THE ARTERIOLES OF THE SKIN IN ESSENTIAL HYPERTENSION[1,2]

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It is generally accepted that a diffuse disturbance of the arterial side of the vascular system exists in hypertension. Curiously enough, the cutaneous arteriolar beds in people with essential hypertension have not been studied adequately. For this reason, we felt that a controlled study of the arteriolar bed of the skin in a group of persons who had essential hypertension might be of value.

REVIEW OF STUDIES

It is of interest to know that in 1868 Johnson (1) reported a study concerning the status of the arterioles in ten patients who had chronic Bright's disease. He found hypertrophy of the arteriolar walls in the kidney, intestines, skeletal muscle, pia mater and *skin*. He interpreted the hypertrophy as being a result of "long continued overactivity of the vessel. . . . " In 1872, Gull and Sutton (2) studied the arterioles and small arteries of fifty-four patients who had chronic Bright's disease. These authors noted considerable changes in these vessels in the kidney, pia mater, *skin*, stomach, spleen, heart, lungs and retina. Thickening of the wall of the vessel, and reduction in diameter of the lumen, were the salient changes. No changes were observed in the larger arteries.

The first study concerning the status of cutaneous vessels in "genuinen Hypertonie" was carried out by Fahr (3), who studied the arterioles of the skin in fifty-three cases. Pieces of skin were removed from the extremities, but most of the specimens of skin taken for biopsy were from the thighs. Fahr observed in this study that the arterioles of the skin and muscles were almost always free

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of change, or that, if some change in the arteriole occasionally is present, the change is very slight.

Watanabe (4) studied specimens of skin from the upper arm, calf, chest and foot obtained at 116 necropsies. The blood pressures of the persons concerned were not recorded. Watanabe found arteriosclerotic changes in the cutaneous vessels in only six instances. His study showed that arterioles of the skin seldom show the arteriosclerotic changes as the medium and large arteries do. This was his only conclusion. He did not discuss the subject of hypertension.

In 1925, Fishberg (5) said that "the terminal arterioles of the *skin*, skeletal muscles, myocardium, lungs, gastro-intestinal tract and thyroid are rarely involved in the arteriosclerotic process, and then only to an insignificant extent." Fishberg examined the cutaneous arterioles in seventeen cases; in no instance was arteriolosclerosis noted. Bell and Clawson (6) observed that "arteriolar changes in the muscle and skin occurred very rarely only." They quoted Watanabe, Fahr and Fishberg in support of this observation.

Of fundamental interest is the work of Kernohan, Anderson and Keith (7). In their study of fifty-two patients who had essential hypertension, biopsy of specimens of pectoral muscle was performed. Twenty-three patients of this group had malignant hypertension, eighteen had early malignant hypertension and eleven had benign hypertension. The fundamental arteriolar changes consisted of hypertrophy of the media and proliferation of the intima of the arteriole. Additional changes which they found in the arterioles were medial thickening (apparently brought about by an increase in the nuclear elements), hypertrophy of the intimal elastic lamina, proliferation of the lining endothelial cells, marked reduction in the size of the lumens of the arterioles and occasional thrombotic occlusion.

These investigators wrote that *a diffuse disturbance of the arterial side of the vascular system exists in hypertension.* In normal persons the wall-to-lumen ratio of the arteriole in the pectoral muscle was approximately 1:2. In twenty-three patients who had malignant hypertension the ratio was 1:1.1. Kernohan, Anderson and Keith postulated that the presence or absence of the lesion in the arterioles may determine the diagnosis and prognosis in individual cases.

An opposite point of view has been expounded by Andrus (8). He believed that the appearance of thickened arteriolar walls was caused by a state of contraction of the arterioles. Because of this he abandoned attempts to measure the wall-to-lumen ratio. "It should be remembered that a state of contraction of the arteriole may make the vessel appear to have a thickened wall."

However, in very thorough and exhaustive reports, Moritz (9), and Moritz and Oldt (10,11) acknowledged that there are contradictory reports concerning the significance of generalized thickening of the walls of small arteries and arterioles in association with arterial hypertension. They proved that variations in technical procedures involved in the fixing, dehydrating and embedding of tissues preliminary to microscopic examination would not produce variations in the relative thickness of the walls of vessels. Physiologic contraction or dilatation of vessels at the time of death was not rendered permanent by fixation of the

tissues. Microscopic studies of the skeletal muscle of dogs were made before and after the administration of vasoconstricting and vasodilating drugs. Neither vasodilation nor vasoconstriction persisted throughout the process of preparation of the tissue for microscopic examination. They concluded that "no significant alteration in the ratio of the internal to the external diameter of arteriolar walls could be related to artifact or the physiologic state of the vessel."

Moritz and Oldt found that the walls of the arterioles from the pectoral muscle of hypertensive persons were thicker than those of persons in the control group, although this finding was not constant in all persons who were known to have had long-standing hypertension. There was hyperplasia of the smooth muscle cells

TABLE 1

Mean ratio of wall of arterioles to lumen, different regions of the body, as reported in various studies

AUTHORS	REGION	RATIO				
		Normal persons	Persons with hypertension of group			
			I	II	III	IV
Kernohan, Anderson, Keith (7)	Pectoral muscle	1:2.00				1:1.1
Morlock (18)	Pancreas	1:2.45				1:1.24
	Liver	1:2.31				1:1.14
	Gastro-intestinal tract	1:2.13				1:1.14
	Spleen	1:1.32				1:1.04
Odel (16)	Myocardium	1:2.00				1:1.88
Rosenberg (12)	Brain	1:3.50				1:1.70
Kyser (14)	Thyroid	1:1.68	1:1.64	1:1.59	1:1.57	1:1.30
Cain (20)	Kidney	1:1.82				1:0.70
Present authors	Skin	1:2.14	1:1.54	1:1.68	1:1.54	1:1.38

in arterioles which were only slightly thickened, and there were degeneration and hypertrophy of the media and intima in arterioles affected by advanced thickening.

Studies have been made, by various workers, of the arterioles in the pectoral muscle (7, 11), brain (12, 13), thyroid (14), myocardium (15, 16), abdominal viscera (17, 18) and the kidney (19, 20) (table 1 and fig. 1).

Morlock found that the arterioles of the pancreas, liver, gastro-intestinal tract and spleen showed no measurable changes in the walls from youth to old age. Marked measurable thickening of the arteriolar wall and reduction of the wall-to lumen ratio as compared to normal were found in hypertensive patients of all

ages. The changes were proportional to the degree of hypertension. All arterioles were not equally affected, but all showed some degree of change from that considered normal. Hyperplasia of nuclear elements appeared to be the earliest histologic change, whereas thickening of the wall was the most common change.

Odel (15, 16) found that myocardial arterioles showed structural changes similar to those occurring in the pectoral muscle of hypertensive persons. However, the changes were inconstant and less pronounced.

Rosenberg (12, 13) found the cerebral arterioles to be profoundly altered in cases of malignant hypertension. This alteration took the form of an increase in the thickness of the walls, with reduction of the caliber of the lumens.

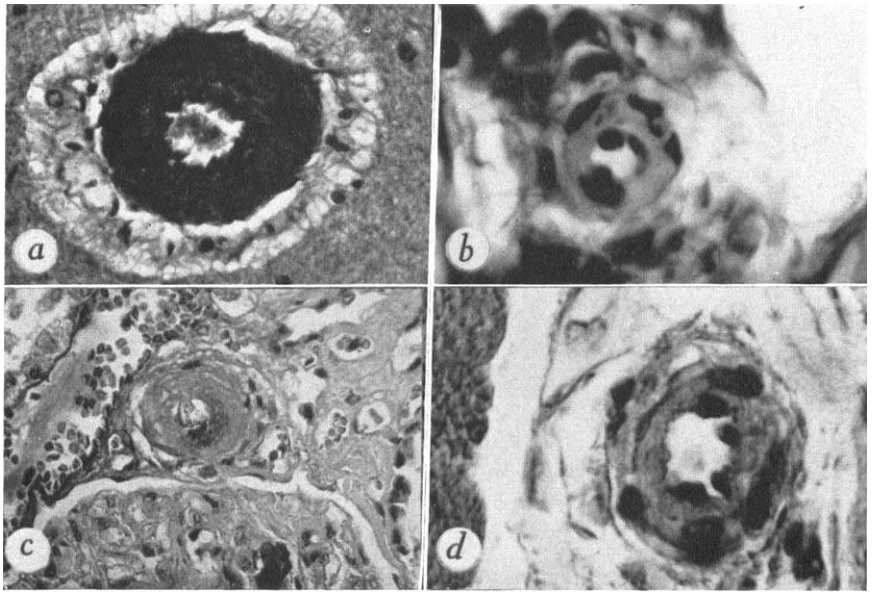

FIG. 1*a*. Arteriole from the brain of a person who had malignant hypertension (hematoxylin and eosin ×300 [from Rosenberg (13)]); *b*, arteriole from the thyroid gland of a person who had essential hypertension (hematoxylin and eosin ×750 [from Kyser (14)]); *c*, arteriole from the kidney of a person who had essential hypertension (hematoxylin and eosin ×300 [from Cain (19)]); *d*, arteriole from the myocardium of a person who had essential hypertension group IV (hematoxylin and eosin ×780 [from Odel (15)]).

Careful review of the literature did not produce any information concerning the wall-to-lumen ratio of cutaneous arterioles in normal persons or in persons with essential hypertension. We have communicated with Drs. Felix Pinkus (21), Fred Weidman (22) and others for information concerning the wall-to-lumen ratio of the cutaneous arterioles; they replied that to their knowledge there have not been previously any studies of the cutaneous arterioles from this standpoint. Lewis (23) stated that the vessels below and including the subpapillary plexus do not lend themselves to physiologic investigation. Steele and Kirk (24) reported that the temperature of the skin of persons suffering from arterial hypertension does not differ from that of the skin of normal persons.

BLOOD SUPPLY OF THE SKIN

Arteries and veins in the skin and subcutaneous tissue do not differ in any respect from from arteries and veins in other organs. Arteries and arterioles possess a plainly developed media containing muscle cells and elastic tissue (fig. 2), whereas veins of equal size either have no muscle layer or have only a very thin one. The medial wall of a vein is composed of connective tissue and an abundant supply of elastic tissue. The investigations of Spalteholz (25) have shown that the skin is supplied by "skin-muscle" arteries and "skin arteries." A "skin-muscle" artery supplies a muscle with blood, but the end part of the artery reaches the skin. A "skin artery" arises from middle or small-sized arteries, such

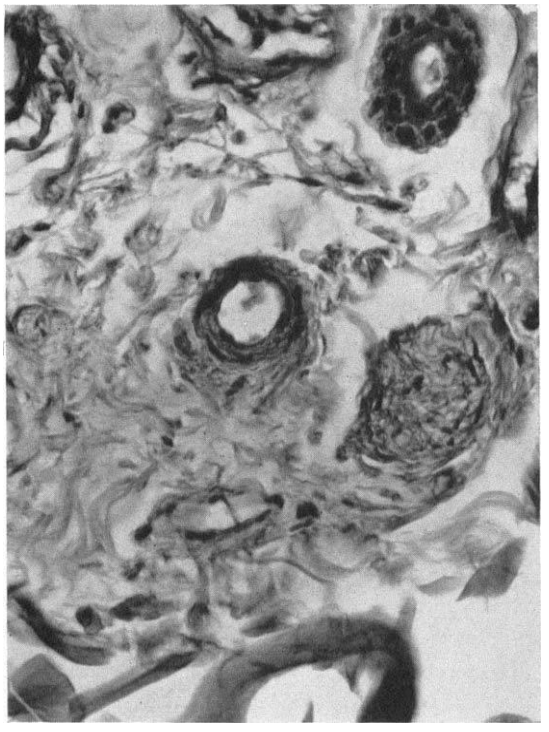

FIG. 2. Cutaneous arteriole from the lumbar region of a person who had normal blood pressure. Cross diameter of this normal arteriole is 50 microns (hematoxylin and eosin ×435).

as the superficial epigastric artery, and penetrates the muscle; it lies under or over its fascia and runs a parallel course to the surface of the skin.

The blood vessels of the subcutaneous tissue are more numerous on the flexor than on the extensor surfaces. Areas of pressure, such as the palms of the hands, the soles of the feet and the gluteal area, are richer in blood vessels than are extensor surfaces. Veins of the subcutaneous tissue may have thick walls and may be mistaken for arteries unless special stains are used.

The skin has a rich vascular network. Two large arteriolar plexuses or networks are present. The larger of the two is situated in the deepest portion of the cutis just above the subcutaneous tissue. This plexus (the cutaneous arterial plexus) is parallel to the surface of the skin, and from it arterioles run vertically and branch horizontally to form a second plexus at the junction of the middle and outer thirds of the cutis (the subpapillary plexus).

Numerous small branches arise from the subpapillary network and run as terminal arterioles toward the epidermis. Most of these branches turn and course for a short distance parallel to the surface of the epidermis, sending their twigs to the arterial limbs of the capillary loops lying in the papillae.

Spalteholz, as quoted by Lewis, has shown that: "The arteries of the cutaneous network possess a thick muscular coat which diminishes relatively abruptly about the middle of the corium where the vessels are clothed by a single layer of muscle cells." It is important to emphasize that *arterioles with a strong muscular coat lie deep to the subpapillary arteriolar plexus*. The vessels of the subpapillary plexus and the terminal arterioles may possess but a slight covering of muscular elements.

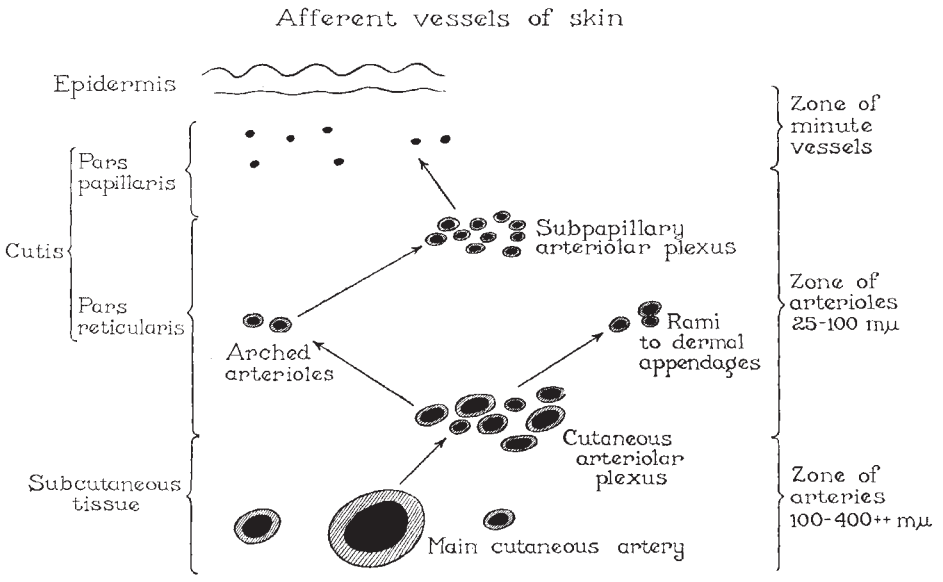

FIG. 3. Diagrammatic representation of relative location and size of afferent vessels in the skin.

Lewis tabulated the afferent vessels of the skin as follows:

- Main cutaneous arteries
- Cutaneous arterial network } strong arterioles
- Arched arterioles
- Branches of the arched arterioles
- Subpapillary arterial network
- Terminal arterioles } minute vessels
- Capillaries

Figure 3 is a diagrammatic sketch of the afferent vessels of the skin. Capillaries and precapillary arterioles are found in the zone of so-called minute vessels, but usually are less than 25 microns in diameter.

METHOD

In order to determine the degree of thickening of the arteriolar walls and the alteration in the diameter of the lumens, measurements were made according to the method followed by Kernohan, Anderson and Keith (7) in their study of the arterioles of the pectoral muscle. A Bausch and Lomb micrometer eyepiece

was used over a high-power objective, which produced a magnification of 430 times (43 × 10). With this instrument the average diameter of the wall of the vessel and of the lumen was measured (fig. 4). Four arterioles were measured in each case. Dr. Berkson, of the Division of Biometry and Medical Statistics of the Mayo Clinic, advised us to measure the first four arterioles we saw in each case under study; in this way a biased study could be avoided. Therefore, we studied every slide from left to right, and made measurements of the first four arterioles we saw in each slide.

In the material obtained for biopsy from people who had normal blood pressure, fewer arterioles were apparent than in the material secured from members of the hypertensive group. It is conceivable that hypertensive arterioles of the skin

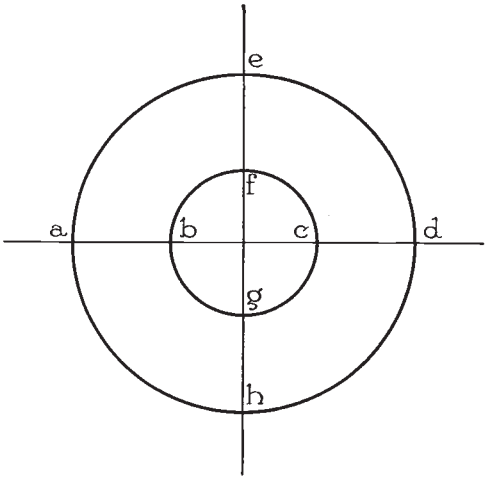

FIG. 4. The diameter of the wall is obtained by dividing the summation of a–b, c–d, e–f, and g–h by 4. The diameter of the lumen is obtained by dividing the summation of b–c and f–g by 2.

are so tortuous that the same vessel may be sectioned several times in one preparation (fig. 5*a*).

MATERIAL

Material for this study was obtained from the upper arm, lumbar region and the calf of fifty-two persons who had normal blood pressure and from seventy persons who had moderate to severe essential hypertension. The skin was obtained by means of excision and punch. All the material in the hypertensive group was secured from living people. The youngest hypertensive person was twenty-nine years old; the oldest person was eighty years old; the mean age was forty-four years. Of the fifty-two specimens of skin removed from persons who had normal blood pressure, forty were taken from living people and twelve were obtained at necropsy.

The Section on Pathologic Anatomy sent us specimens of skin from the upper arm (at the junction with the shoulder girdle), and from the leg, obtained from the twelve persons with normal blood pressure who came to necropsy. The relative wall-to-lumen ratio of vessels in the skin obtained from postmortem material was essentially the same as the wall-to-lumen ratio of vessels in skin secured from living patients with normal blood pressure.

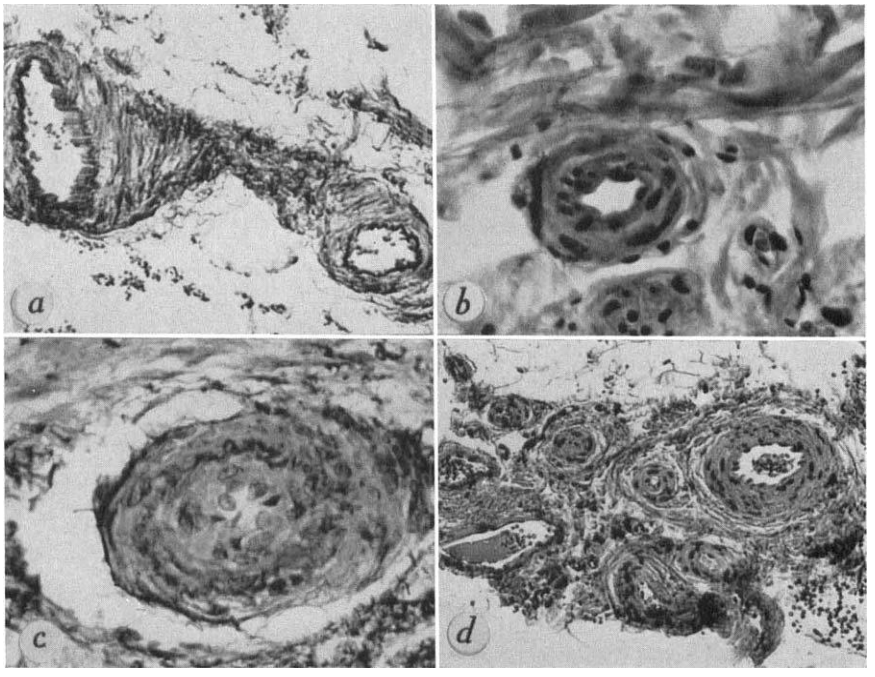

FIG. 5*a*. Tortuous arteriole in the lower portion of the cutis from skin removed from the left calf of a forty-one year old woman who had long-standing essential hypertension (elastin-H ×120); *b*, cutaneous arteriole from the leg of a forty-five year old woman who had group III essential hypertension: the lumen is narrowed and there are thickening of the arteriolar wall and an apparent increase in the number of cells in the media; this arteriole is located in the midportion of the pars reticularis, and its cross diameter is 50 microns (hematoxylin and eosin ×435); *c*, cutaneous arteriole from the leg of a fifty-five year old woman who had long-standing group I essential hypertension: the lumen is almost completely obliterated and there are proliferation of the endothelial cells of the intima and thickening of the inner elastic lamina; the cross diameter of this arteriole is 75 microns (elastin-H ×435); *d*, cluster of arterioles in the deep portion of the cutis from skin removed from the left calf of a thirty-four year old man who had group II essential hypertension (hematoxylin and eosin ×125).

All tissue was fixed in formaldehyde U.S.P. (1:10), blocked in paraffin and stained. Four stains were used: hematoxylin and eosin stain, elastin-H stain, van Gieson stain and the elastin-van Gieson stain (26).

It is well known that a chronic inflammatory reaction may produce thickening of the arteriolar wall. Hence, only normal-appearing skin was studied.

The adventitia was not included in determination of the outer diameter of the arteriole. In this study, the outermost cells of the media were used to define the external diameter.

There is no widely accepted definition of an arteriole. Maximow and Bloom (27) referred to arterioles as "the smallest arteries, i.e. 300 microns or smaller." Evans (28) defined an arteriole as an artery with a media of two to three muscle cells in thickness. Kernohan and associates used the measurements of 25 to 100 microns to delimit the arterioles in their study. We have employed their criteria, and have measured vessels with diameters in this range. Most of the arterioles were located in the deeper portion of the cutis. Not infrequently, arterioles varying from 25 to 40 microns were found adjacent to dermal appendages.

QUALITATIVE CHANGES OF ARTERIOLES AMONG HYPERTENSIVE PERSONS

Although thickening is characteristic of the hypertensive arteriole, it was not present in nine of our seventy patients who had essential hypertension. This observation parallels the findings of Moritz and Oldt (11), who also observed normal arterioles in some persons who had long-standing elevation of the blood pressure. It was apparent that the arterioles of hypertensive patients have thicker walls than are those of nonhypertensive patients. Careful study of each arteriole revealed structural changes similar to those found in the arterioles in other organs of persons with hypertension. Endothelial hyperplasia, proliferation and thickening of the inner elastic lamina were frequently present. Hyperplasia of nuclear elements in the media also was present. A reduction in the size of the lumen, periarteriolar fibrosis and occasional thrombotic occlusion likewise were observed (fig. 5*b*, *c* and *d*).

We did not make a statistical analysis of the qualitative changes in the arterioles. In this study it was apparent that not all arterioles were equally affected; nonetheless, a large percentage showed some change from the so-called normal arteriole. In our series there was no appreciable difference in a comparison of the wall-to-lumen ratio of the arterioles of the group in the third to fourth decade and the group in the sixth to seventh decade of life. This also is in conformity with results of most of the investigations of arterioles in other organs in the hypertensive group.

RATIO OF WALL TO LUMEN OF THE NORMAL ARTERIOLE

Cutaneous arterioles from the arm, leg and back of fifty-two persons who had normal blood pressure were measured. The mean age of these patients was forty-four years; sixteen were women, thirty-six were men.

Skin from the arm.—The lowest wall-to-lumen ratio was 1:1.39; the highest ratio was 1:3.00; the average was 1:2.13.

Skin from the leg.—The lowest wall-to-lumen ratio was 1:1.43; the highest was 1:2.63; the average was 1:2.10.

Skin from the lumbar region.—The lowest wall-to-lumen ratio was 1:1.28; the highest was 1:2.66; the average was 1:2.20.

Mean.—The mean for the control group was 1:2.14 (table 1). These results are practically identical with the normal values other workers have found. Kernohan, Anderson and Keith considered the ratio 1:2.00 to be normal for arterioles in all tissues (table 1).

RATIO OF WALL TO LUMEN AMONG HYPERTENSIVE PERSONS

Cutaneous arterioles from the arm, leg and back of seventy patients who had essential hypertension were measured. The average age of these patients was forty-four years; thirty-five were women and thirty-five were men.

TABLE 2

Mean ratio of the thickness of the wall to the diameter of the lumen of the arterioles of normal and hypertensive persons

BIOPSY, SITE	NORMAL PERSONS		HYPERTENSIVE PERSONS	
	Number	Mean wall-to-lumen ratio	Number	Mean wall-to-lumen ratio
Arm	25	1:2.13	15	1:1.53
Leg	14	1:2.10	21	1:1.29
Back	13	1:2.20	34	1:1.76
All sites	52	1:2.14	70	1:1.57

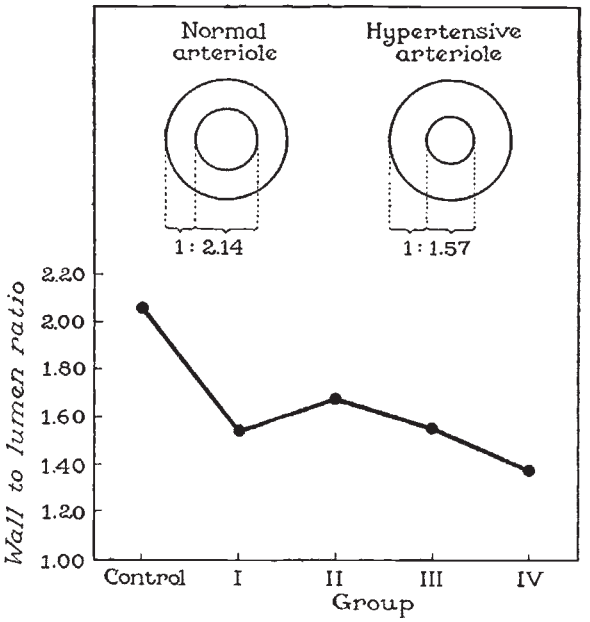

FIG. 6. Graphic representation of the relationship of the wall-to-lumen ratio to the group of hypertension.

Skin from the arm.—The lowest wall-to-lumen ratio was 1:0.82; the highest was 1:1.99; the average was 1:1.53.

Skin from the leg.—The lowest wall-to-lumen ratio was 1:0.87; the highest was 1:1.69; the average was 1:1.29.

Skin from the lumbar area.—The lowest wall-to-lumen ratio was 1:1.12; the highest was 1:2.78; the average was 1:1.76 (table 2).

TABLE 3

Age of normal and hypertensive patients and mean ratio of thickness of wall to diameter of lumen of arterioles

AGE	NORMAL PERSONS		HYPERTENSIVE PATIENTS	
	Number	Mean wall-to-lumen ratio	Number	Mean wall-to-lumen ratio
years				
10–19	1	1:2.27	0	
20–29	7	1:2.17	3	1:2.21
30–39	9	1:2.08	17	1:1.68
40–49	15	1:2.18	32	1:1.59
50–59	14	1:2.22	11	1:1.44
60–69	3	1:1.87	5	1:1.09
70–79	2	1:1.95	1	1:1.21
80–89	1	1:2.01	1	1:1.70

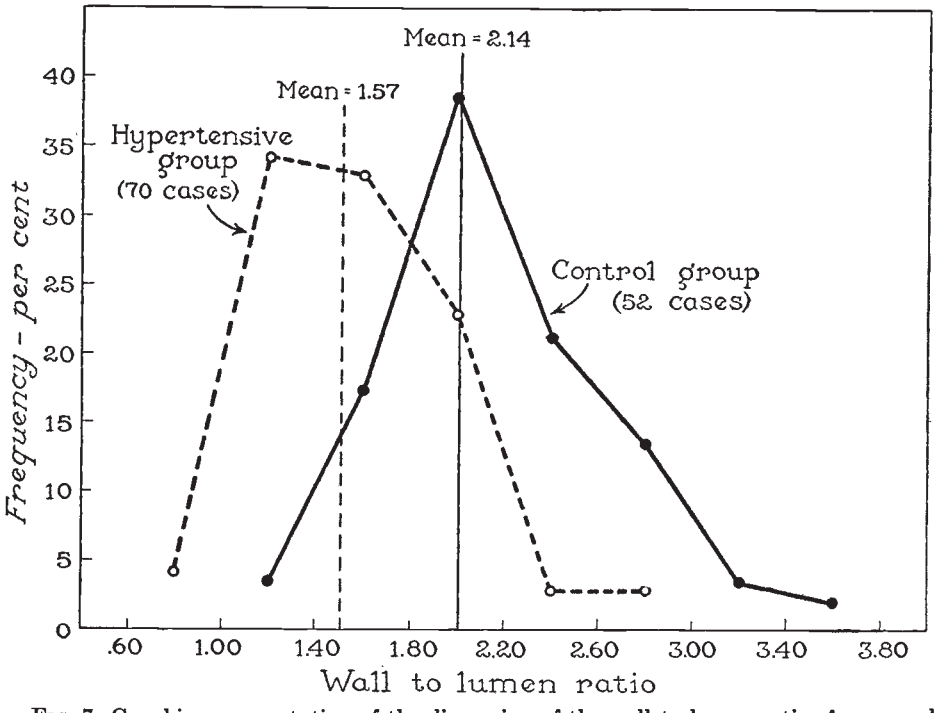

FIG. 7. Graphic representation of the dispersion of the wall-to-lumen ratios for normal and hypertensive persons. There is overlapping of the ratios in the hypertensive and normal groups.

Mean.—The mean for seventy cases was 1:1.57. The arterioles of the patients who had group IV hypertension were more profoundly altered than were those of patients who had hypertension of other groups (fig. 6). Thirteen patients had hypertension of group I, thirty-one had hypertension of group II, sixteen had hypertension of group III, ten had hypertension of group IV.

COMMENT

Although the arterioles in the skin of persons who had malignant hypertension were more profoundly altered than were those of persons who had other types of hypertension, equally severe qualitative changes were present in the arterioles of a number of persons who had the other types of hypertension. The duration and severity of the hypertension, as well as the fact that only one small portion of skin is under study, are variables which may influence the degree of arteriolar change.

Andrus (8) and others have shown that the severity of arteriolosclerosis in hypertensive persons is not directly proportional to age. Arterioles of the hypertensive patients and of those in the control series did not show any measurable difference in the wall-to-lumen ratio from youth to old age (table 3).

Moritz and Oldt found arteriolosclerosis in some nonhypertensive persons. In one study they reported that 12 per cent of nonhypertensive persons had renal arteriolosclerosis. Arteriolosclerosis is present in organs other than the kidney in nonhypertensive persons. In our group of normal controls there were four cases in which the wall-to-lumen ratio was decreased and medial hypertrophy was present. This suggests that arteriolosclerosis was present in approximately 5 per cent of members of the control group in this study. Figure 7 represents a dispersion of the wall-to-lumen ratio of arterioles of both normal and hypertensive persons, and shows that this ratio overlaps in respect to arterioles of hypertensive patients and normal patients.

Conversely, nine of the hypertensive patients did not have arteriolosclerosis, nor was there any decrease in the wall-to-lumen ratio of their arterioles.

CONCLUSIONS

A measurable thickening of the arteriolar wall and a decrease in the wall-to-lumen ratio as compared to normal were found in vessels of the skin of hypertensive patients. The average of the wall-to-lumen ratio of the arterioles of fifty-two persons with normal blood pressure was 1:2.14; among seventy persons who had essential hypertension it was 1:1.57. All arterioles were not equally affected in the same case.

Qualitative changes also were present. Hyperplasia of the nuclear elements of the media and thickening of the inner elastic lamina appeared to be the most common changes. Occasionally, complete occlusion of the lumen occurred. Four patients with normal blood pressure had medial hypertrophy of the arteriolar wall.

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REFERENCES

1. JOHNSON, GEORGE: On certain points in the anatomy and pathology of Bright's disease of the kidney. II. On the influence of the minute blood-vessels upon the circulation. Med.-Chir. Tr., Lond., **51**, 57, 1868.

2. GULL, W. W., AND SUTTON, H. G.: On the pathology of the morbid state commonly called chronic Bright's disease with contracted kidney ("arterio-capillary fibrosis"). Med.-Chir. Tr., Lond., **55**, 273, 1872.
3. FAHR, T.: Über die Beziehungen von Arteriolensklerose, Hypertonie und Herzhypertrophie. Virchows Árch. f. path. Anat., **239**, 41, 1922.
4. WATANABE, SUSUMU: Ueber die Arteriosklerose der Hautgefässe. Schweiz. med. Wchnschr., **51**, 780, 1921.
5. FISHBERG, A. M.: Anatomic findings in essential hypertension, Arch. Int. Med., **35**, 650, 1925.
6. BELL, E. T., AND CLAWSON, B. J.: Primary (essential) hypertension; a study of four hundred and twenty cases. Arch. Path., **5**, 939, 1928.
7. KERNOHAN, J. W., ANDERSON, E. W., AND KEITH, N. M.: The arterioles in cases of hypertension. Arch. Int. Med., **44**, 395, 1929.
8. ANDRUS, F. C.: The relation of age and hypertension to the structure of the small arteries and arterioles in skeletal muscle. Am. J. Path., **12**, 635, 1936.
9. MORITZ, A. R.: Arteriolar changes in essential hypertension. Science, **80**, 547, 1934.
10. MORITZ, A. R., AND OLDT, MARY R.: Arteriolar changes in essential hypertension. Am. J. Path., **11**, 885, 1935.
11. MORITZ, A. R., AND OLDT, M. R.: Arteriolar sclerosis in hypertensive and non-hypertensive individuals. Am. J. Path., **13**, 679, 1937.
12. ROSENBERG, E. F.: The brain in malignant hypertension. Proc. Staff Meet., Mayo Clin., **14**, 217, 1939.
13. ROSENBERG, E. F.: The brain in malignant hypertension. Thesis, Graduate School, University of Minnesota, 1941.
14. KYSER, F. A.: Relationship of essential hypertension to pathologic changes in the thyroid gland. Thesis, Graduate School, University of Minnesota, 1940.
15. ODEL, H. M.: A study of the changes in the arterioles of the myocardium in a group of cases of diffuse arteriolar disease with hypertension, Group IV. Thesis, Graduate School, University of Minnesota, 1937.
16. ODEL, H. M.: Arteriolar changes in the myocardium in diffuse arteriolar disease with hypertension, Group IV. Proc. Staff Meet., Mayo Clin., **14**, 210, 1939.
17. MORLOCK, C. G.: The arteriole of the pancreas, liver, gastro-intestinal tract, and spleen in hypertension. Thesis, Graduate School, University of Minnesota, 1937.
18. MORLOCK, C. G.: Arterioles of the pancreas, liver gastrointestinal tract and spleen in hypertension. Arch. Int. Med., **63**, 100, 1939.
19. CAIN, E. F.: An investigation of the histologic changes in the kidneys of a group of cases of diffuse arterial disease with hypertension, Group 4. Thesis, Graduate School, University of Minnesota, 1933.
20. CAIN, E. F.: Malignant hypertension: the histologic changes in the kidneys. Arch. Int. Med., **53**, 832, 1934.
21. PINKUS, FELIX: Personal communication to the authors.
22. WEIDMAN, FRED: Personal communication to the authors.
23. LEWIS, THOMAS: The Blood Vessels of the Human Skin and Their Responses. Chicago, Chicago Medical Book Company, 1927, pp. 1–7.
24. STEELE, J. M., AND KIRK, ESBEN: The significance of the vessels of the skin in essential hypertension. J. Clin. Investigation, **13**, 895, 1934.
25. SPALTEHOLZ, WERNER: Anatomie der Haut. In: Handbuch der Haut- und Geschlechtskrankheiten. Berlin, Julius Springer, 1927, vol. 1, pt. 1, p. 401.
26. MALLORY, F. B.: Pathological Technique. Philadelphia, W. B. Saunders Company, 1938, p. 170.
27. MAXIMOW, A. A., AND BLOOM, WILLIAM: A Textbook of Histology, Ed. 3. Philadelphia, W. B. Saunders Company, 1938, 668 pp.
28. EVANS, GEOFFREY: A contribution to the study of arterio-sclerosis, with special reference to its relation to chronic renal disease. Quart. J. Med., **14**, 215, 1921.

DISCUSSION

Dr. Hermann Pinkus: This excellent paper should not go without discussion. Dr. Farber has opened a new field of study in the skin, and has demonstrated that diligent microscopic research still has its place in dermatology. I should like to ask Dr. Farber to clarify two points on which he did not elaborate.

1. I noticed that biopsies were taken from the arm, the lumbar region, or the leg, and I wonder if several sites were examined in the same individual, and if regional differences were found. From my own experience in routine biopsy material, I should expect to find thicker arteriolar walls in the leg than in other portions of the body.

2. How does the local anesthetic influence the arterioles? The blood vessels of hypertonic persons not only have thicker walls, but are more apt to be contracted and are thrown into spasm more easily. Could it be that the injected mixture of anesthetic and adrenalin causes a stronger contraction in hypertonic patients than in normal individuals, and that some of the thickening may be apparent rather than real?

Closing discussion by Dr. E. M. Farber: I wish to thank Dr. Pinkus for raising some questions which are of fundamental importance in this study. Multiple specimens of the skin were taken for biopsy from the same person. We did not present the figures now because of the limitation of time, but these will be presented in the paper.

Local anesthesia is not a cause of alteration of the arteriolar wall. Some of the material for this study was obtained at the time of sympathectomy and some skin was obtained at necropsy. There was no difference in the wall-to-lumen ratio of the arterioles in the skin removed, ante mortem or post mortem, from patients who had normal blood pressure and patients who had elevated blood pressure.

Physiologic contraction or dilatation of vessels is not rendered permanent by fixation of tissues. Moritz and Oldt[1] in their study showed that the administration of vasodilating and vasoconstricting drugs does not produce arteriolar changes which persist throughout the process of fixation. Spasticity, therefore, is not a cause of a decrease in the size of the arteriolar lumen.

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[1] Moritz, A. R. and Oldt, M. R.: Arteriolar sclerosis in hypertensive and non-hypertensive individuals. Am. J. Path. **13**: 679–728 (Sept.) 1937.